K082340

Elecsys Folate III Test System (including RBC Folate Hemolyzing Reagent)

# 510(k) Summary

**Introduction**

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

**Submitter name, address, contact**

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JUN 19 2009

Date Prepared: July 25, 2008

**Device Name**

Proprietary names: (1) Elecsys Folate III
(2) Elecsys RBC Folate Hemolyzing Reagent
(3) Elecsys Folate III CalSet
(4) Elecsys Folate III CalCheck
(5) Elecsys PreciControl Anemia

Common names: (1) Folate III
(2) RBC Folate
(3) Folate III CalSet
(4) Folate III CalCheck
(5) PreciControl Anemia

Classification names: (1) Folic Acid Test System
(2) Folic Acid Test System
(3) Calibrator
(4) Quality Control Material (Assayed and Unassayed)
(5) Quality Control Material (Assayed and Unassayed)

Product codes: (1) CGN
(2) CGN
(3) JIT
(4) JJX
(5) JJY

**Device Description**

(1) The Elecsys Folate III assay employs a competitive test principle using natural folate binding protein (FBP) specific for folate. Folate in the sample competes with the added folate (labeled with biotin) for the binding sites on FBP (labeled with ruthenium complex). Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

(2) The Elecsys RBC Folate Hemolyzing Reagent is a 0.2% ascorbic acid solution with which whole blood treated with anticoagulants (heparin or EDTA) is diluted. After incubation the erythrocytes are lysed and intracellular folate is liberated and stabilized. The hemolysate is then used as a prediluted sample for subsequent measurement in the Elecsys Folate III assay.

(3) The Elecsys Folate III CalSet is a lyophilized product consisting of human serum with folic acid in two concentration ranges. During manufacture, the analyte is spiked into the matrix. This calibrator is used to calibrate the Elecsys Folate III assay.

(4) Elecsys Folate III CalCheck is a lyophilized product consisting of human serum with folic acid. During manufacture, the analyte is spiked into the matrix. This solution is used to verify the calibration established with the Elecsys Folate III CalSet.

(5) The Elecsys PreciControl Anemia is a lyophilized control serum based on human serum matrix in three concentration ranges. The controls are used for monitoring the accuracy and precision of the Elecsys Ferritin, Folate III, and Vitamin B12 immunoassays.

**Intended use**

**Folate III:**

Binding assay for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers.

**RBC Folate Hemolyzing Reagent:**

Elecsys RBC Folate Hemolyzing Reagent is used together with the Elecsys Folate III assay for the quantitative determination of folate in erythrocytes (RBC (red blood cell) folate). Binding assay for the in vitro quantitative determination of folate in human serum and plasma. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers.

**Folate III CalSet:**

Elecsys Folate III CalSet is used for calibrating the quantitative Elecsys Folate III assay on the Elecsys and cobas e immunoassay analyzers.

**Folate III CalCheck:**

Elecsys Folate III CalCheck is used for the verification of the calibration established by the Elecsys Folate III reagent on the indicated Elecsys and cobas e immunoassay analyzers.

**PreciControl Anemia:**

Elecsys PreciControl Anemia is used for the quality control of Elecsys immunoassays on Elecsys and cobas e immunoassay analyzers.

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**Indications for Use**

**Folate III and RBC Folate Hemolyzing Reagent:** Measurements obtained by these devices are used in the diagnosis and treatment of anemias.

**Folate III CalSet**: Elecsys Folate III CalSet is used for calibrating the quantitative Elecsys Folate III assay on the Elecsys and cobas e immunoassay analyzers.

**Folate III CalCheck:** Elecsys Folate III CalCheck is used for the verification of the calibration established by the Elecsys Folate III reagent on the indicated Elecsys and cobas e immunoassay analyzers.

**PreciControl Anemia:** Elecsys PreciControl Anemia is used for the quality control of specified Elecsys immunoassays on Elecsys and cobas e immunoassay analyzers.

**Substantial equivalence**

The Elecsys Folate III Test System is substantially equivalent to the Elecsys Folate II Test System. This test system includes the following 5 components which have been cleared under the following K numbers:

1) Elecsys Folate II (K043318)
2) Elecsys RBC Hemolyzing Reagent (K051292)
3) Elecsys Folate II CalSet II (K042490)
4) Elecsys Folate II CalCheck II (K043320)
5) Elecsys PreciControl Anemia (K051517)

(The original Elecsys Folate Assay was cleared under K973674.)

## 510(k) Summary, Continued

**Substantial equivalence – comparison**

| Elecsys Folate III Reagent | | |
|---|---|---|
| **Feature** | **Elecsys Folate III Assay** | **Predicate Device: Elecsys Folate II Assay (K043318)** |
| Intended Use | Binding assay for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers. | Binding assay for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers. |
| Indication for Use | This assay may be used as an aid in the diagnosis and treatment of anemias. | This assay may be used as an aid in the diagnosis and treatment of anemias. |
| Assay Protocol | Electrochemiluminescent Immunoassay | Electrochemiluminescent Immunoassay |
| Sample Type | Serum (tubes containing separating gel can be used) | Serum (tubes containing separating gel can be used) |
| Labeled Instrument Platform | Roche Elecsys 2010/ **cobas e** 411 and MODULAR ANALYTICS E170 (Elecsys module)/ **cobas e** 601 analyzers. | Roche Elecsys 2010/ **cobas e** 411 and MODULAR ANALYTICS E170 (Elecsys module)/ **cobas e** 601 analyzers. |
| Calibrator | Elecsys Folate III CalSet | Elecsys Folate II CalSet II |
| Calibration frequency | Once per reagent lot and<br>• After 1 month when using same reagent lot<br>• After 7 days when using same reagent kit<br>• As required per QC findings or pertinent regulations | Once per reagent lot and<br>• After 1 month when using same reagent lot<br>• After 7 days when using same reagent kit<br>• As required per QC findings or pertinent regulations |
| Controls | PreciControl Anemia | PreciControl Anemia |
| Traceability | This method has been standardized against the Elecsys Folate II assay | This method has been standardized against the Elecsys Folate assay |

Elecsys Folate III Test System (including RBC Folate Hemolyzing Reagent)

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| Reagent Stability | Unopened 2-8°C – up to expiration<br>Opened 2-8°C – **8 weeks**<br>On Elecsys 2010 and cobas e411– 2 weeks | Unopened 2-8°C – up to expiration<br>Opened 2-8°C –12 weeks<br>On Elecsys 2010 and cobas e411– 2 weeks |
| Measuring Range | 1.5 - 20.0 ng/mL | 0.600 - 20.00 ng/mL |
| Precision | **Elecsys 2010 and cobas e411 Total Precision**<br>(range of values)<br>• PreciControl Anemia 2: SD 0.467 ng/mL; CV 6.4%<br>• PreciControl Anemia 3: SD 0.986 ng/mL; CV 6.3%<br>• Human Samples < 10 ng/mL, CV 7.0-13.3%<br>• Human Samples > 10 ng/mL, CV 5.0% | **Elecsys 2010 and cobas e411 Total Precision**<br>(range of values)<br>• PreciControl Universal 1: SD 0.82 ng/ml; CV 6.8%<br>• PreciControl Universal 2: SD 0.50 ng/ml; CV 7.9%<br>• Human Samples < 10 ng/mL, CV 6.1-13.8%<br>• Human Samples > 10 ng/mL, CV 7.0% |
| Analytical Sensitivity | Limit of Blank = ≤0.640 ng/mL<br>Limit of Detection = ≤1.5 ng/mL<br>Limit of Quantitation = ≤2.0 ng/mL | Lower Detection Limit = 0.6 ng/mL |
| Analytical Specificity | The following cross-reactivities were found:<br>Aminopterin 2.7%<br>Folinic acid 2.3%<br>Amethopterin 2.3% | Same |

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| Interferences | • The assay is unaffected by icterus (bilirubin < 564 µmol/L or < 33 mg/dL), lipemia (Intralipid < 1500 mg/dL), and biotin < 86.1 nmol/L or < 21 ng/mL, IgG < 16 g/L and IgA < 4.0 g/L.<br>*Criterion: Recovery within ± 10% of initial value with samples >5 ng/mL and ≤ +/- 0.5 ng/mL with samples ≤ 5 ng/mL.*<br>• In patients receiving therapy with high biotin doses (i.e. >5 mg/day), no sample should be taken until at least 8 hours after the last biotin administration.<br>• No interference was observed from rheumatoid factors up to a concentration of 1000 IU/mL.<br>• In vitro tests were performed on 18 commonly used pharmaceuticals and in addition on human erythropoietin. No interference with the assay was found.<br>• It is contraindicated to measure samples of patients receiving therapy with certain pharmaceuticals, e.g. methotrexate or leucovorin, because of the cross-reactivity of folate binding protein with these compounds.<br>• In rare cases, interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur. | • The assay is unaffected by icterus (bilirubin < 684 µmol/L or < 40 mg/dL), lipemia (Intralipid < 1500 mg/dL), and biotin < 123 nmol/L or < 30 ng/mL, IgG < 16 g/L and IgA < 4.0 g/L.<br>*Criterion: Recovery within ± 10% of initial value.*<br>• In patients receiving therapy with high biotin doses (i.e. >5 mg/day), no sample should be taken until at least 8 hours after the last biotin administration.<br>• No interference was observed from rheumatoid factors up to a concentration of 1000 IU/mL.<br>• In vitro tests were performed on 56 commonly used pharmaceuticals and in addition on human erythropoietin. No interference with the assay was found.<br>• Folate assays of samples from patients receiving therapy with certain pharmaceuticals, e.g. methotrexate or leucovorin, are contraindicated because of the cross-reactivity of folate binding protein with these compounds.<br>• In rare cases, interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur. |
| Dilution | Sample measuring >20ng/mL can be manually diluted and a dilution factor of 2 applied | Sample measuring >20ng/mL can be manually diluted and a dilution factor of 2 applied |
| Expected Values | American Journal of Clinical Nutrition<br>Expected = 4.6 – 34.8 ng/mL<br>(all ages & male/female) | New England Journal Of Medicine<br><br>Expected = 3.1 – 17.5 ng/mL |

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| Method Comparison | A comparison of the Elecsys Folate III assay (Elecsys 2010 Immunoassay analyzer) and the Elecsys Folate II assay (Elecsys 2010 Immunoassay analyzer) where N=98<br><br>Sample concentrations were between approx. 1.76 and 15.9 ng/mL<br><br>Passing/Bablock:<br>Slope = 1.13<br>Y intercept = -0.10<br>tau = 0.833<br><br>Linear Regression<br>Slope = 1.13<br>Y intercept = -0.06<br>r=0.962 |

| (2) Elecsys RBC Folate Hemolyzing Reagent | | |
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| **Feature** | **Elecsys RBC Folate Hemolyzing Reagent** | **Predicate Elecsys RBC Folate Hemolyzing Reagent (K051292)** |
| Intended Use/Indications for Use | Elecsys RBC Folate Hemolyzing Reagent is used together with the Elecsys Folate III assay for the quantitative determination of folate in erythrocytes (RBC folate) on the Elecsys 2010/cobas e 411 analyzers. | Elecsys RBC Folate Hemolyzing Reagent is used together with the Elecsys Folate II assay for the quantitative determination of folate in erythrocytes (RBC folate). |
| Expected Values | Study in the USA using the Elecsys Folate III assay the cobas e411 Immunoassay analyzer, N=262:<br><br>(Values corrected for hematocrit)<br><br>Median – 902 ng/mL<br><br>2.5$^{th}$97.5$^{th}$ percentile – 499-1504 ng/mL | Study in the USA using the Elecsys Folate III assay on the Elecsys 2010 and cobas e411 Immunoassay analyzers, N=121:<br><br>(values corrected for hematocrit)<br><br>Median – 790 ng/mL<br><br>2.5$^{th}$97.5$^{th}$ percentile – 496-1477 ng/mL |
| Precision | **Total Precision (n=84)**<br><br>(values <u>not</u> corrected for hematocrit)<br><br>**2010/cobas e411 Analyzer**<br>7.0% CV @ 229 ng/mL<br>7.2% CV @ 350 ng/mL<br>7.2% CV @ 481 ng/mL | **Total Precision (n=63)**<br><br>(values corrected for hematocrit)<br><br>**2010/cobas e411 Analyzer**<br>6.8% CV @ 478 ng/mL<br>6.6% CV @ 573 ng/mL<br>5.5% CV @ 623 ng/mL |
| Measuring Range | 46.5 – 572 ng/mL<br><br>The lower end of the measuring range is derived from the lower end of the serum folate test. Values are not corrected for hematocrit. | Without consideration for hematocrit, up to 620 ng/mL<br><br>(derived from the upper limit of the serum folate test) |

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| Method Comparison | A comparison of the Elecsys RBC Folate together with the Elecsys Folate III assay (Elecsys 2010/cobas e411 analyzer; calibrated with Elecsys Folate III CalSet: y) and the Elecsys RBC Folate with the Elecsys Folate II assay (Elecsys 2010/cobas e411 analyzer: calibrated with Elecsys Folate II CalSet II; x) where N=98<br><br>(Values were not corrected for Hematocrit)<br><br>Sample concentrations were between approx. 123 and 566 ng/mL<br><br>Passing/Bablock:<br>Slope = 1.096<br>tau = 0.700<br><br>Linear Regression<br>Slope = 1.019<br>r = 0.921 | |
| Dilution | Sample measuring >20ng/mL can be manually diluted and a dilution factor of 2 applied | Sample measuring >20ng/mL can be manually diluted and a dilution factor of 2 applied |

| **(3) Elecsys Folate III CalSet** | | |
|---|---|---|
| **Feature** | **Elecsys Folate III CalSet** | **Predicate Elecsys Folate II CalSet II (K042490)** |
| Intended Use | Elecsys Folate III CalSet is used for calibrating the quantitative Elecsys Folate III assay on the Elecsys and cobas e immunoassay analyzers. | Elecsys Folate II CalSet II is used for calibrating the quantitative Elecsys Folate II assay on the Elecsys and cobas e immunoassay analyzers. |
| Levels | Two | Two |
| Matrix | Human serum preserved with 0.5% Bronidox L and buffered with 50mM HEPES | Human serum |
| Format | Lyophilized | Lyophilized |
| Stability | Unopened: up to the stated expiration date<br>After reconstituting:<br>At 2-8C – 3 days<br>At -20C – 3 months (freeze only once)<br>Onboard: use only once | Unopened: up to the stated expiration date<br>After reconstituting:<br>At 2-8C – 3 days<br>At -20C – 3 months (freeze only once)<br>Onboard: use only once |

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|---|---|---|
| Composition | **Buffer:** HEPES 50mM<br><br>**Preservative:** Bronidox L 0.5% | No buffer or preverative in composition |

| (4) Elecsys Folate III CalCheck | | |
|---|---|---|
| **Feature** | **Elecsys Folate III CalCheck** | **Predicate Elecsys Folate II CalCheck II (K043320)** |
| Intended Use | For use in the verification of the calibration established by the Elecsys Folate III reagent on the indicated Elecsys and cobas e immunoassay analyzers. | For use in the verification of the calibration established by the Elecsys Folate II reagent on the indicated Elecsys and cobas e immunoassay analyzers. |
| Levels | Three | Three |
| Matrix | Human serum preserved with 0.5% Bronidox L and buffered with 50mM HEPES | Human serum |
| Format | Lyophilized | Lyophilized |
| Stability | Unopened and stored at 2-8C: up to the stated expiration date<br>After reconstituting: 4 hours at 20-25C | Unopened and stored at 2-8C: up to the stated expiration date<br>After reconstituting: 4 hours at 20-25C |
| Composition | **Buffer:** HEPES 50mM<br><br>**Preservative:** Bronidox L 0.5% | No buffer or preverative in composition |

| (5) Elecsys PreciControl Anemia | | |
|---|---|---|
| **Feature** | **Elecsys PreciControl Anemia** | **Predicate Elecsys PreciControl Anemia (K051517)** |
| Intended Use | Elecsys PreciControl Anemia is used for quality control of Elecsys immunoassays on the Elecsys and cobas e immunoassay analyzers. | Elecsys PreciControl Anemia is used for quality control of the Elecsys Ferritin, Folate II, and Vitamin B12 immunoassays. |
| Levels | Three | Three |
| Matrix | Human serum | Human serum |
| Format | Lyophylized | Lyophilized |

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| Stability | Unopened: up to the stated expiration date<br>After reconstituting:<br>At 20-25C: up to 8 hours<br>On board at 20-25C: up to 5 hours<br>At 2-8C: 3 days<br>At -20C: 1 month (freeze only once)<br>After thawing: use only once | Unopened: up to the stated expiration date<br>After reconstituting:<br>At 20-25C: up to 8 hours<br>On board at 20-25C: up to 5 hours<br>At 2-8C: 3 days<br>At -20C: 1 month (freeze only once)<br>After thawing: use only once |

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 19 2009

Ms. Kathie Goodwin
Roche Diagnostics Corp.
9115 Hague Rd.
Indianapolis, IA
46250

Re: k082340
Trade/Device Name: Roche Elecsys Folate III, Roche Elecsys RBC Folate Hemolysing Reagent, Roche Elecsys Folate III CalSet, Roche Elecsys Folate III CalCheck, Roche Elecsys PreciControl Anemia
Regulation Number: 21 CFR 862.1295
Regulation Name: Folic Acid Test System
Regulatory Class: Class II
Product Code: CGN, JIT, JJY, JJX
Dated: June 11, 2009
Received: June 16, 2009

Dear Ms. Goodwin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Courtney C. Harper, Ph.D.
Acting Director
Division of Chemistry and Toxicology
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

# Indications for Use Form

510(k) Number (if known): K082340

Device Name: (1) Elecsys Folate III
(2) Elecsys RBC Folate Hemolyzing Reagent
(3) Elecsys Folate III CalSet
(4) Elecsys Folate III CalCheck
(5) Elecsys PreciControl Anemia

Indications for Use:

**(1) Elecsys Folate III:** Binding assay for the in vitro quantitative determination of folate in human serum and plasma. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers. Measurements obtained by these devices are used in the diagnosis and treatment of anemias. For in vitro diagnostic use.

**(2) Elecsys RBC Folate Hemolyzing Reagent:** Elecsys RBC Folate Hemolyzing Reagent is used together with the Elecsys Folate III assay for the quantitative determination of folate in erthrocytes (RBC (red blood cell) folate). Binding assay for the in vitro quantitative determination of folate in human serum and plasma. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers. Measurements obtained by these devices are used in the diagnosis and treatment of anemias.

**(3) Elecsys Folate III CalSet**: Elecsys Folate III CalSet is used for calibrating the quantitative Elecsys Folate III assay on the Elecsys and cobas e immunoassay analyzers.

**(4) Elecsys Folate III CalCheck:** Elecsys Folate III CalCheck is used for the verification of the calibration established by the Elecsys Folate III reagent on the indicated Elecsys and cobas e immunoassay analyzers.

**(5) Elecsys PreciControl Anemia:** Elecsys PreciControl Anemia is used for the quality control of specified Elecsys immunoassays on Elecsys and cobas e immunoassay analyzers.

Prescription Use ___X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

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Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K082340